LETTER TO THE EDITOR

Erythema multiforme after CoronaVac vaccination

Dear Editor,

In January 2021, SARS-CoV-2 vaccine, CoronaVac, developed by Sinovac Life Sciences (Beijing, China) was approved for the use in Brazil by its National Health Surveillance. It is an inactivated SARS-CoV-2 virus adsorbed on aluminium hydroxide and diluted in sodium chloride and phosphate-buffered saline.[1] Like other novel vaccines against COVID-19, it can induce cutaneous adverse reactions, generally mild.[1] Erythema multiforme (EM) is an acute and usually self-limited immune-mediated mucocutaneous disorder.[2] It is related to infections in 90% of cases – mainly herpes simplex virus (HSV) infections – and in 10% of cases, to drugs.[2] Unusually, it has also been documented following the vaccination.[3] We report a case of EM after CoronaVac vaccination.

A 75-year-old man with hypertension received both doses of the COVID-19 vaccine, CoronaVac: the first on February 12th and the second on March 6th. He was also in the use of ramipril 5 mg for the past 7 years. He had no adverse reactions after the first dose. However, five days after the second dose, he started with pruriginous, raised edematous lesions, with two colour zones and poorly defined borders, symmetrically in his knees (Fig. 1) that then spread to his face (Fig. 2) and trunk. He denied systemic symptoms, intake of new medications, and had no signs suggesting any infections. Mucous membranes were not affected. Also, he had neither medical history of herpes simplex infections, nor cutaneous adverse reactions to previous vaccines. A punch biopsy was performed and showed a lymphohistiocytic infiltrate surrounding the superficial dermal vessels. Laboratory tests, like erythrocyte sedimentation rate, white blood cell count, liver enzyme levels and serologies, were normal. A diagnosis of erythema multiforme minor was made, and treatment with topical corticosteroids and oral antihistamines for symptomatic relief was performed.

Almost, all vaccine components can be potential triggers to allergic reaction, but they are usually caused by the inert

Figure 1 Erythematous, slightly violaceous, raised, edematous plaques, with two color zones and poorly defined borders on the left knee.

Figure 2 Round erythematous papules on the forehead.

components (excipients).[4] Adjuvants, like aluminium salt present in CoronaVac, are responsible for type IV hypersensitivity.[4] Polyethylene glycol (macrogol), in the currently available Pfizer (New York, NY, USA)-BioNTech (Mainz, Germany) and Moderna, was suggested to cause immediate hypersensitivity reactions and also delayed-type reactions like pseudoallergic or non-IgE-mediated urticaria.[4,5]

Recently, EM was registered after mRNA-based COVID-19 vaccines: three cases after Moderna first dose[6] and a case of EM-like lesions in a patient with lupus erythematosus (Rowell's syndrome) after Pfizer first dose.[7] But until now, we have no data about EM after the CoronaVac vaccine. Although a fortuitous occurrence cannot be totally excluded in our case, the temporal association, absence of HSV infection history and other identifiable triggers make very likely the eruption, was caused by CoronaVac.

The aetiology of EM is unclear, but appears that in genetically predisposed individuals, and a trigger (usually infection) induces cell-mediated immune processes against antigens, via CD4 type 1 T-helper cells, release of IFN-γ and then recruitment of autoreactive T cells.[3] IFN-γ was also detected as an indicator of T-cell responses after CoronaVac vaccination.[1] Hence, we hypothesize that CoronaVac can act as an inciting factor that activates the same pathway of EM leading to a type III or IV of hypersensitivity either by the vaccine itself or to its components.[8]

Erythema multiforme following vaccination is rare, just as other major adverse events and should not discourage the use of vaccines. Also, the rarity of the disease makes it hard to establish a causal link. But since we are just at the beginning about learning of the novel anti-SARS-CoV-2 vaccines, it is important to be aware about its possible cutaneous adverse reactions.

Conflict of Interest

None declared.

Consent statement

The patient authorized the release of the photographs and the clinical case for scientific purposes.

Ethical principles

This paper contains a small case report and respects the ethical principles for medical research.

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